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CARDIAC FUNCTION AND HEART FAILURE

ANGIOTENSIN RECEPTOR BLOCKERS IMPROVED CARDIOMYOGENIC TRANSDIFFERENTIATION EFFICIENCY OF HUMAN MARROW-DERIVED MESENCHYMAL STEM CELLS IN VITRO

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Background: Human marrow-derived mesenchymal stem cell (MSC) might not be a good cardiac stem cell source, because of low cardiomyogenic transdifferentiation efficiency (CTE) of MSC and modest efficacy of MSC transplantation. However, if they can be improved, MSC may come back to be a good stem cell source again. Since angiotensin plays an important role in maintenance of cardiomyocyte homeostasis and angiotensin receptor blockers (ARBs) shows favorable effect on patient with cardiovascular disease, we hypothesized that ARB might affect CTE of MSC.

Methods: EGFP-labeled MSCs were co-cultured with murine fetal cardiomyocytes for cardiomyogenic induction (CI). Immediately before CI, MSCs were pretreated with 3μM of ARBs (PD123319, valsartan, olmesartan, losartan, candesartan, telmisartan) for 2 weeks. Few days after CI, EGFP-positive MSCs start beating. One week after CI, MSCs were stained immunocytochemically, and CTE was defined as the ratio of anti-cardiac troponin-I positive cells in the EGFP-positive cells.

Results: MSC-derived cardiomyocteys stained positive for troponin-I (with clear striation pattern) by immunocytochemical method. Pretreatment with ARBs significantly increased the CTE (Fig), while PD123319, a specific AT2 receptor blocker, did not affect the CTE.

Conclusions: The pretreatment of MSCs with ARB significantly improved CTE via blockade of AT1 receptor. ARB-activated MSCs can be a promising cellular source for cardiac stem cell therapy.